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09/509,188	06/05/2000	JAN DROUAUD	065691/0184	8841

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/509,188	Applicant(s) DROUAUD ET AL.	
	Examiner Stuart Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-10, and 12-17 including SEQ ID NO:3 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that Applicants believe that claim 18, directed to a vector of claim 4, added in a Preliminary Amendment filed August 18, 2000, should be added to Group I.

Claim 18 has been added.

The requirement is still deemed proper and is therefore made FINAL.

Claim 11 has been cancelled.

Claims 1-10 and 12-18 will be examined on their merits.

Claims 12 and 16 are objected to for misspelling "Brassicaceae".

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 23 September, 1997. It is noted, however, that applicant has not filed a certified copy of the French application as required by 35 U.S.C. 119(b).

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: Specifically, the first page of the specification should be amended to indicate that the application is a 371 of PCT/FR98/02042 filed 23 September, 1998.

This application, filed under former 37 CFR 1.60, lacks formal drawings. The informal drawings filed in this application are acceptable for examination purposes. When the application

is allowed, applicant will be required to submit new formal drawings. In unusual circumstances, the formal drawings from the abandoned parent application may be transferred by the grant of a petition under 37 CFR 1.182.

The U.S. patents listed on form 1449 have not been considered as they were not provided by the Applicant. As stated in the MPEP § 1.98 (a) Any information disclosure statement filed under § 1.97 shall include: (1) A list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) A legible copy of:

(i) Each U.S. patent application publication and U.S. and foreign patent;

(ii) Each publication or that portion which caused it to be listed;

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, and 12-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a nucleotide sequence comprising SEQ ID NO:3 or a sequence comprising nucleotides 1 to 2111 of SEQ ID NO:3, or any sequence from any source that hybridizes to or exhibits 80% homology to said sequences, and a vector comprising one of said sequences upstream of a nucleic acid encoding a cytotoxic product, and a plant exhibiting

male sterility comprising a gene encoding a cytotoxic product, and a method for producing a gametophytic male sterile plant comprising said vector, and a method wherein said cytotoxic product is a subtilisin protease.

The Applicants isolated their invention from a subtraction hybridization between cDNA libraries constructed from fertile floral tissue of rape and male sterile rape. Putative clones were used to screen a microspore library and one of the resulting clones was used to screen a genomic library purchased from CLONETECH Laboratories, Inc. Clone BnM3.2 (SEQ ID NO:3) was isolated and the promoter sequence was used to construct a cassette comprising said promoter sequence and the beta-glucuronidase gene. Transformation experiments with said construct yielded plants exhibiting GUS expression specifically in the microspores.

The Applicants do not identify structural features unique to SEQ ID NO:3, the functional domains of the sequence nor the overall function of the sequence. In addition, the Applicants do not specify nor describe a gene encoding a male-gamete-specific cytotoxic product nor do they describe a subtilisin protease. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for SEQ ID NO:3 or any nucleic acid encoding a cytotoxic product or a subtilisin, it remains unclear what features identify SEQ ID NO:3 or any nucleic acid encoding a cytotoxic product or

a subtilisin including any sequence exhibiting the first 2111 nucleotides of SEQ ID NO:3 or any sequence that is 80% homologous to said sequences or hybridizes to it under conditions of unspecified stringency, or any sequence encoding a cytotoxic product or encoding a subtilisin. Since SEQ ID NO:3 or any nucleic acid encoding a cytotoxic product or a subtilisin protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

Claims 1-10, and 12-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a nucleotide sequence comprising SEQ ID NO:3 or a sequence comprising nucleotides 1 to 2111 of SEQ ID NO:3, or any sequence from any source that hybridizes to or exhibits 80% homology to said sequences, and a vector comprising one of said sequences upstream of a nucleic acid encoding a cytotoxic product, and a plant and plant cells transformed with said vector, and a plant exhibiting male sterility with inducible fertility comprising a gene encoding a male gamete-specific cytotoxic product, and a method for producing a gametophytic male sterile plant comprising said vector and further comprising inhibiting the cytotoxicity of the gene product in an inducible manner, thereby producing plants that are able to self-fertilize, and a method wherein said cytotoxic product is a subtilisin protease.

The Applicants isolated their invention from a subtraction hybridization between cDNA libraries constructed from fertile floral tissue of rape and male sterile rape. Putative clones were used to screen a microspore library and one of the resulting clones was used to screen a genomic

library purchased from CLONETECH Laboratories, Inc. Clone BnM3.2 (SEQ ID NO:3) was isolated and a segment of the promoter sequence was used to construct a cassette comprising said promoter segment and the beta-glucuronidase gene. Transformation experiments with said construct yielded plants exhibiting GUS expression specifically in the microspores.

The Applicants are claiming a sequence of DNA that expresses in microspores and methods of making male sterile plants but Applicant has only demonstrated that a piece of DNA 2056 base pairs long can specify GUS expression in microspores. Applicant has not demonstrated that SEQ ID NO:3 or sequences that are 80% homologous or that hybridize under conditions of unspecified stringency to SEQ ID NO:3 or nucleotides 1 to 2111 of SEQ ID NO:3 or sequences that are 80% homologous or that hybridize to said subsequence of SEQ ID NO:3 will still specify expression in microspores. And in addition, Applicants have not demonstrated that operably linking one of these sequences to a gene encoding a protease or subtilisin will disrupt the normal development of the microspores so that they do not develop further into pollen grains. And further, Applicants have not demonstrated that the supposedly male-sterilizing construct can be nullified so that male fertile gametes are produced. Lastly, Applicants have not taught or demonstrated that a promoter operably linked to a cytotoxic product can be induced by applying to the plant an insecticide molecule of the fluorophosphates family.

Non-coding nucleic acid sequences that exhibit base pair deletions, substitutions or rearrangements, cannot be expected to maintain their promoter or enhancer activity. Izawa et al (1993, J. Mol. Biol. 230 :1131-1144) teach that the nucleotides flanking the G-box (CACGTC) and C-box (GACGTC) hexameric cores were shown to affect protein binding activity and specificity of bZIP transcription factors (page 1132, bottom of right column; page 1134, bottom

of left column). Hao, et al (1998, The J. of Biological Chemistry 273 (41): 26857-26861) investigated the binding activities of ethylene-responsive element-binding proteins (EREBP) to their cis-element GCC box (AGCCGCC). Creating base-pair substitutions within the GCC box modulates binding specificity, implying that different positions within the GCC box are important for differential binding by different EREBP's, in particular, substituting T's for the two G's eliminates binding completely (*supra*, pages 26857, abstract and 26860, left column, 2nd paragraph).

Even though the Applicant is not utilizing intronic regions to help specify microspore expression, the molecular mechanism of transcription for intronic regions is the same as 5' promoter regions. Busch et al (1999, Science 285:585-587) and Lohmann et al (2001, Cell 105 :793-803) teach that *LEAFY* (*LFY*) and *WUSCHEL* (*WUS*), which have been shown to be transcription factors that together activate proper *AGAMOUS* (*AG*) expression, do so by binding to the second intron of the *AG* gene. A two base-pair mutation within the binding site of either *LFY* or *WUS* eliminates binding of either *LFY* or *WUS*, respectively (Busch et al (supra) page 587 left column, 2nd paragraph; Lohmann et al (supra) page 799, bottom and top of left and right columns) and changes the temporal and spatial *AG* expression pattern.

Applicant's proposed use of subtilisin to produce male-sterile plants will not produce the expected result. Taylor et al (1997, The Plant Journal 12(6):1261-1271) teach that a serine proteinase which is a member of the subtilisin-related proteins (page 1268, left column, last paragraph) is detected in both tapetal cells of the anther and in microsporocytes (page 1268, left column, 2nd paragraph). Given that the Applicants want to express a subtilisin in microsporocytes for the purpose of rendering the microsporocyte non-viable and therefore

creating male-sterile plants, it is unclear how expressing a protein which is already present in the microsporocytes to begin with will have an adverse effect on the developmental biology of the microsporocyte. In addition, not all subtilisin proteins are alike. Jorda et al (2000, Plant Physiology 122 :67-73) teach that there are five distinct subfamilies of subtilase genes in plants (page 67, right column, 1st paragraph). Jorda et al teach that the P69E and P69F genes which are members of the p69 family, have different developmental roles compared to other family members (page 72, right column, 3rd paragraph).

Given the unpredictability of creating a male-sterile plant using a promoter fragment other than the 2056 base pairs of SEQ ID NO:3, and the unpredictability of using a protease, in particular a subtilisin protease for the reasons stated above, and the unpredictability of using an insecticide molecule of the fluorophosphates family to induce the expression of a cytotoxic product; given the lack guidance and working examples for using a sequence other than the 2056 base pairs of SEQ ID NO:3 operably linked to a nucleic acid encoding a cytotoxic product or a sequence other than the 2056 base pairs of SEQ ID NO:3 operably linked to a nucleic acid encoding a subtilisin wherein the expression of the subtilisin is induced by applying an insecticide molecule for the reason stated above; given the state of the prior art which does not provide further guidance about isolating promoter regions with the same expression profile as the 2056 base pairs of SEQ ID NO:3 and which does not provide further guidance about using an insecticide molecule to induce the expression of a gene and which does not provide further guidance about using subtilisin as a cytotoxic product with which to kill microsporocytes, it would require undue experimentation by one skilled in the art to make and/or use the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 5-9, and 13-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Cigan et al (filed Jan. 7, 1995, U.S. Patent Number 5,689,049)

The claims are drawn to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID NO:3 or a sequence which hybridizes to one of the above-sequences under conditions of unspecified stringency, or a fragment thereof of any length. The claims are drawn to a plant having gametophytic male sterility with inducible fertility and seeds thereof, and a method for producing a plant with gametophytic male sterility with inducible fertility comprising transforming a plant with a vector comprising a gene whose product is cytotoxic to microspores and operably linking said gene to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID

NO:3 or a sequence which hybridizes to one of the above-sequences under conditions of unspecified stringency, or a fragment thereof. Claims 7-9 are drawn to a plant comprising a gene encoding any male gamete cytotoxic product, and claims 7-8 additionally do not recite any particular promoter.

Cigan et al teach a method of producing male sterile plants comprising transforming a plant with an expression vector comprising a methylase gene operably linked to a promoter that specifically directs expression in the anthers. Promoter methylation by the methylase gene can cause gene inactivation and alter the phenotype in transgenic organisms (column 3, 5th paragraph) and as such will act as a cytotoxin to disrupt the normal development of the cell in which the methylase is expressed. Cigan et al also teach a method for reversing the infertility caused by the methylase gene by including in the promoter operably linked to the methylase gene an operator sequence on which binds a LexA repressor (column 5; 2nd paragraph). The gene encoding the LexA repressor is operably linked to an inducible promoter and transformed into plants comprising the methylase construct. Seeds of the transformed plants are produced (column 23,lines 36-47) and plants are multiplied by allowing regenerated plants to self or by crossing regenerated plant to a suitable plant of the same species using breeding methods known to those of skill in the art (column 22, lines 58-61). Having both the methylase and LexA constructs in one plant creates a plant and method for inducing male sterility and given that a promoter with an A, T, G, or C reads on a "fragment" as claimed by Applicant, which would also hybridize to SEQ ID NO:3 or portions thereof under conditions of low stringency, Cigan et al anticipate the claimed invention.

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Sim et al (filed June 7, 1995, U.S. Patent Number 5,993,827).

The claims are drawn to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID NO:3 or a sequence which hybridizes to one of the above-sequences, or a fragment thereof.

Sim et al teach a DNA sequence that exhibits 3.6% identity with SEQ ID NO:3. Given the wording of the claim, i.e., a sequence that hybridizes under unspecified conditions to SEQ ID NO:3 or a fragment thereof, any sequence that shares at least one base pair with SEQ ID NO:3 or derivatives thereof, would be encompassed by the claim and as such, Sim et al anticipate the claimed invention.

Claims 1-3, 5-9, 12-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Mariani et al (U.S. Patent Number 5,689,041, filed February 28, 1995).

The claims are drawn to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID NO:3 or a sequence which hybridizes to one of the above-sequences under conditions of unspecified stringency, or a fragment thereof of any length. The claims are drawn to a plant having gametophytic male sterility with inducible fertility and seeds thereof, and a method for producing a plant with gametophytic male sterility with inducible fertility comprising transforming a plant with a vector comprising a gene whose product is cytotoxic to microspores and operably linking said gene to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID NO:3 or a sequence which hybridizes to one of the above-sequences under conditions of

unspecified stringency, or a fragment thereof wherein the plant is in the Brassicaceae family in particular a rape plant, including a seed from a before-mentioned plant. Claims 7-9 are drawn to a plant comprising a gene encoding any male gamete cytotoxic product, and claims 7-8 additionally do not recite any particular promoter.

Mariani et al teach a barnase gene which encodes a cytotoxic product, which comprises a fragment thereof that reads on Applicant's claimed sequences, as a fragment can be interpreted as comprising one base pair of DNA. Mariani et al also teach plants transformed with this gene and the barstar gene which deactivates the barnase protein and plants having gametophytic male sterility with inducible fertility and methods of producing these plants (column 7, lines 9-15; column 22, Example 7; column 31, claim 1) wherein the plants are in the Brassicaceae family, in particular, rape plants (column 32, claim 17). Mariani also teach a method of reproducing these plants as discussed in columns 14-19 and as such anticipate the claimed invention.

Claim 18 is rejected under 35 U.S.C. 102(a) as being anticipated by Ballinger et al (1996, Biochemistry 35:13579-13585).

The claim is drawn to a vector comprising a nucleotide sequence as described in previous 102 rejection and a cytotoxic product wherein the cytotoxic product is subtilisin.

Ballinger et al teach a vector comprising a nucleotide sequence encoding a subtilisin operably linked to a promoter for expression in E. coli wherein the promoter would comprise a fragment of the claimed invention given that a fragment can be defined as a single base pair, and as such, Ballinger et al anticipate the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 14 is drawn to a seed of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed progeny (seeds), it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy , Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of the claims to recite that the seeds comprise the construct that was introduced into the parent seed would overcome the rejection.

Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The nucleic acid sequence reads on naturally occurring nucleic acid since it has not been isolated. Amend claims 1-2 to insert --An isolated-- before "nucleotide sequence" in line 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al(filed February 28, 1995) taken with Ramjee et al (1996, Protein Engineering 9:1055-1061).

The claims are drawn to a vector comprising to a nucleotide sequence comprising SEQ ID NO:3 or a sequence which stretches from nucleotide 1 to 2111 of SEQ ID NO:3 or a sequence which hybridizes to one of the above-sequences under conditions of unspecified stringency, or a fragment thereof of any length wherein the sequence is upstream of a DNA sequence encoding a cytotoxic product wherein the cytotoxic product is a protease.

Mariani et al teach a vector comprising a promoter sequence that would comprise a fragment of the claimed invention given that a fragment can be defined as a single base pair. This sequence is operably linked to a cytotoxic product, as discussed above.

Mariani et al do not teach a gene encoding a protease.

Ramjee et al teach an isolated nucleic acid encoding a papain protease from papaya fruit (see e.g., page 1055-1056 of Material and Methods).

Given the recognition of those of ordinary skill in the art of the value of producing a vector comprising a promoter sequence that expresses in stamens operably linked to a cytotoxic product to be used in a method of producing male-sterile plants as taught by Mariani et al, it

would have been obvious to use the method of Mariani et al and to modify this method as suggested by Mariani et al (column 7, lines 9-15) by using a nucleic acid encoding a protease such as papain, and to use the papain protease as taught by Ramjee et al.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4, 7, 9, and 13 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4, 7, and 9 are indefinite in the recitation "cytotoxic product". Applicant has not defined this term and has not defined the metes and bounds of products that would be toxic to plant cells. For example, diptheria toxin is toxic to plant cells only above a certain threshold concentration.

Claim 7 is indefinite and unclear in the recitation "male-gamete-specific cytotoxic product". Applicant has not defined or described a cytotoxic product that is specific to plant male gametes.

Claim 9, lines 2-3 is indefinite and unclear in the recitation "gene is inserted as a a vector". It is unclear how a gene can be inserted as a vector. In addition, one of the "a's" needs

to be deleted. Amending the claim to recite --gene is inserted into a vector-- will rectify the rejection.

Claim 13 is indefinite for reciting "plants obtained in step d) by reproducing steps b) and c)". Applicant has amended claim 9 to no longer recite letters "d)" "b) and c)".

Claim 10 is deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest plant transformation with a subtilisin encoding gene under the control of an insecticide-inducible promoter for the production of male sterility.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015.

Stuart Baum Ph.D.

August 9, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638